REMARKS/ARGUMENTS

Favorable reconsideration and continued examination of the present application are respectfully requested.

In the Office Action of December 22, 2005, claims 9, 13, 15 - 17, 20 - 24, 27, 30, and 31 were rejected. Claim 25 was objected to because it is dependent on a rejected claim. No claim was allowed. In the present amendments to the claims of the application, claims 13, 15, and 21 are canceled and claims 16, 20, and 30 are amended. Claim 16 is amended in order to avoid the duplication of claim 9. Support for the amendments may be found throughout the present specification and claims as originally filed, including, for example, page 7, line 7, to page 8, line 4. Accordingly, no questions of new matter should arise, and entry of the amendment is respectfully requested.

The applicants appreciate the Examiner's acknowledgement of the amendment to the Sequence Listing and withdrawal of the rejections as indicated on pages 2-3 of the Office Action.

Rejection of claims 9, 13, 15 - 17, 20, 21, 24, 27, 30, and 31 under U.S.C. §112, first paragraph

At page 3 of the Office Action, the Examiner still rejects claims 9, 13, 15-17, 20, 21, 24, 27, 30, and 31 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. In the detailed comments on pages 4-5 of the Office Action, which are virtually identical to the comments made in the previous Office Action, the Examiner takes the position that while the specification provides a written description of the RNA higher-order structure that contains one of the sequences of SEQ ID NOs: 1-7 or a sequence containing a

mutation of PKI in the PSIV-IRES to permit translation of a GFP gene, the specification does not provide a written description of the genus of variants for an RNA higher-order structure with PKI, II, and III structures and a function for promoting translation activity or an RNA higher-order structure made up of a base sequence having at least 50% homology to the SEQ ID NOs: 1-7, a complementary strand of the base sequence, a sequence hybridizing to the base sequence under stringent condition or a base sequence that has been mutated or altered. The Examiner responds to the arguments made in the previous response by alleging that the specification does not provide sufficient teachings on the identities of the functional polynucleotides related to the SEQ ID NOs: 1-7 and how to identify functional polynucleotides and numerous polynucleotides related to SEQ ID NOs: 1-7. The Examiner alleges that a person skilled in the art cannot envision all of the contemplated nucleotide sequences or an RNA higher-order structure based upon a specific RNA higher-order structure of PSID-IRES.

The applicants respectfully traverse this rejection.

While applicants believe that the Examiner is in error in making this rejection, in order to expedite prosecution of the present application, independent claims 20 and 30 have been amended as indicated above. The applicants submit that the amendments to claims 20 and 30 overcome this rejection.

Therefore, this rejection should be withdrawn.

Rejection of claim 13 under U.S.C. §112, second paragraph

At page 8 of the Office Action, the Examiner rejects claim 13 as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards

as the invention. In particular, the Examiner alleges that claim 13 is indefinite because the claim, which recites "at least PK (pseudoknot) I, II, and III structures are maintained in the RNA higher-order structure," does not further limit claim 21, which depends on claim 20, and claim 20 requires that the polynucleotide has an RNA higher-order structure including PK I, II, and III structures.

Claim 13 has been canceled by way of this amendment. Therefore, the rejection of this claim is now moot.

Rejection of claims 9, 13, 15, 16, and 20 - 23 under 35 U.S.C. §102(b) over Sasaki et al.

At page 9 of the Office Action, the Examiner continues to reject claims 9, 13, 15, 16, and 20-23 under 35 U.S.C. §102(b) as being anticipated by Sasaki et al. (J. Virology, 73, 1219-1226 (1999)). The Examiner repeats the allegations from the previous Office Action that Sasaki et al. teaches AUG-unrelated translation initiation that is mediated by the IRES of PSIV *in vitro* in that Sasaki et al. teaches that the LUC gene (a heterologous protein) was translated when fused downstream of $IRES_{6201}$ or $IRES_{6264}$ in that $IRES_{6264}$ contains SEQ ID NO: 1. The Examiner further states that although the reference does not specifically indicate that the $IRES_{6201}$ of PSIV has an RNA higher-order structure (PK I, II, or III), the $IRES_{6201}$ sequence contains SEQ ID NO: 1 and has the function of promoting translation activity. Thus, it would be expected that the $IRES_{6201}$ sequence has at least PK I, II, or III structure, and the reference anticipates the claimed invention.

Furthermore, the Examiner states that the previous amendment to claims 20 and 30 does not overcome the rejection. The previous amendment clarifies that in the synthesis of a

heterologous protein or polypeptide, the polynucleotide encoding the heterologous protein or heterologous polypeptide is immediately downstream from the PKI structure of the polynucleotide that promotes translation activity.

Finally, the Examiner alleges that the previous amendment does not overcome the rejection because the reference teaches pCAT-IRES-LUC series of constructs, LUC genes without an AUG initiation codon was ligated to the PSIV sequences (Fig. 5) and the LUC gene was efficiently translated when fused downstream of nt 6201 (pCAT-$IRES_{6201}$-LUC, Fig. 5, lane 4) in vitro. The Examiner therefore alleges that the reference teaches the 3' boundary of the IRES is located between nt 6196 and 6201, which indicates that the IRES extends into the capsid-coding region (page 1222, left column, lines 1-5) and that the $IRES_{6201}$ contains the same SEQ ID NO: 1 as the claimed invention.

The Examiner concludes that since the claims require that the polynucleotide encoding the heterologous protein is immediately downstream from the PKI structure without indicating the nucleotide positions of the PKI structure, and the reference teaches the construct of pCAT-$IRES_{6201}$-LUC, where the 3' boundary of the IRES is located between nt 6196 and 6201, and the $IRES_{6201}$ of PSIV comprises SEQ ID NO: 1, which has a function of promoting translation activity, the polynucleotide of pCAT-$IRES_{6201}$-LUC meets the limitations for the claimed invention. Applicants respectfully traverse this rejection for the following reasons.

The Examiner is in error in making this rejection. Even if Sasaki et al. teaches its IRES extending into the capsid-codon region, this does not mean that it teaches placing a polynucleotide encoding the heterologous protein or heterologous polypeptide immediately downstream of the PKI structure because the IRES encompasses the PKI structure. However, the

amendment to claims 20 and 30 should further overcome this rejection. Claims 20 and 30 now recite SEQ ID NOs: 1-7 in relation to PKI. Therefore, the 3' boundary of the IRES of Sasaki et al. being located between nt 6196 and 6201 cannot be interpreted to meet the claimed invention in the manner in which the Examiner alleges. For these reasons, the rejection should be withdrawn.

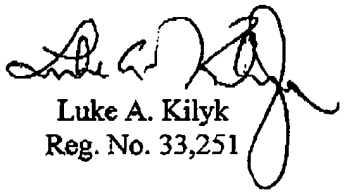
Objection to claim 25

The applicants appreciate the Examiner stating that claim 25 is objected to only because the claim is dependent from rejected claim 20.

Conclusion

If there are any fees due in connection with the filing of this response, please charge the fees to Deposit Account No. 50-0925. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such extension is requested and should also be charged to said Deposit Account.

Respectfully submitted,



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